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10/565,903	06/21/2006	Alessandro Massimo Gianni	3765-0119US1	7353

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EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	**PAPER NUMBER**
1654	

NOTIFICATION DATE	DELIVERY MODE
11/29/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/565,903	GIANNI ET AL.	
	Examiner	Art Unit	
	Ronald T. Niebauer	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,11-14 and 18-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,11-14,18-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants amendments and arguments filed 10/9/07 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Claims 2,6-10,15-17 have been cancelled. Claims 18-26 have been added. Claims 1,3-5,11-14,18-26 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(Necessitated by amendment) **Claim 26** is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New claim 26 is drawn to a kit comprising G-CSF and PlGF packaged for administration.

Lack of Ipsis Verbis Support

The specification is void of any literal support for a kit or for any packaging of compositions. Applicants point to page 5 lines 18-20 for support for a kit. However, page 5 lines 18-20 do not provide any literal support for a kit. Literal support is not found anywhere else in the specification either.

Lack of Implicit or Inherent Support

Section 2163 I-B of the MPEP states, 'while there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure'. However, no express, implicit, or inherent support is provided. Applicants point to page 5 lines 18-20 for support. However, this section of the specification recites that the preparation can be a part of a formulation. New claim 26 specifically states that the kit comprises the composition packaged for administration. There is no support for any type of packaging. The recitation of a formulation does not imply that it is present in a package. The examples provided do not describe making the composition as part of a kit. The examples provided do not describe providing packaging for the composition. Hence, it cannot be said that the original disclosure provides express, implicit, or inherent support for claim 26.

Claim Rejections - 35 USC § 103 (Bahlmann and Robinson)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(Maintained in part/Necessitated by amendment) **Claims 1,3, 11, 13,18-25** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bahlmann et al. (US 2005/0272634, cited previously) in view of Robinson et al. (cited previously).

Since the claims have been amended and new claims have been added, the updated rejection is recited below.

Bahlmann teach pharmaceutical compositions that include PlGF and GM-CSF (claims 41 and 26, section 0075 for example) (compare current claims 1,18-21 (same except G-CSF is used instead of GM-CSF)). Bahlmann teach the pharmaceutical composition for parenteral administration (claim 18, section 0054) (compare current claims 3,13,14,25). Bahlmann teach a method of administering to a patient a composition comprising PlGF and GM-CSF (section 0075, claim 26) (compare current claims 11,22,24 and dependent claims). The composition as used by Bahlmann would involve simultaneous administration since the components are in the same composition (compare current claim 25). Bahlmann teach the method for a range of purposes and patient populations (abstract, sections 0031-0047), such as the mobilization of progenitor cells or stem cells (section 0023). In particular, treatments are described for those about to undergo or who have undergone organ or tissue transplantations (section 0063-0064) (compare current claim 11). Bahlmann specifically teach GM-CSF for stimulating blood cells (section 0006) (compare current claim 24).

Bahlmann et al. does not teach G-CSF, instead Bahlmann teach GM-CSF.

Robinson et al. teach that both GM-CSF and G-CSF have been used for mobilization of stem cells (abstract). Bahlmann also teach the mobilization of stem cells (throughout, section 0023, 0007) and GM-CSF for stimulating blood cells (section 0006). On page 535 (1st paragraph) Robinson teach that GM-CSF and G-CSF (each individually) have been delivered to mobilize stem cells in the clinic. It is also pointed out (page 535 1st paragraph) that 'studies have compared the efficacy of similar daily doses of GM-CSF or G-CSF'. Robinson et al. teach that recombinant versions of G-CSF and GM-CSF are commonly used (abstract)

It has been recently held that "Neither §103's enactment nor *Graham*'s analysis disturbed

the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art." KSR v. Teleflex, 550 U.S. ___, 82 USPQ2d 1385, 1389 (2007). The KSR court stated that "a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR at 1389. The Supreme Court stated that there are "[t]here cases decided after Graham [that] illustrate this doctrine." KSR at 1395. "In United States v. Adams, 383 U.S. 39, 40, 148 USPQ 479 (1966) . . .[t]he Court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result." KSR at 1395. Thus, the mere substitution of one known element for another to obtain a predictable result is obvious.

Furthermore, The KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case, the recognized problem in the art is the mobilization of cells (see Robinson abstract and Bahlmann section 0007, 0023). PlGF and GM-CSF are obvious to try as part of the composition and for the patient populations taught by Balhmann from the finite number of active ingredients taught by Bahlmann in, for example, claim 41. Further, since GM-CSF and G-CSF were known to be used for the same purpose (see Robinson discussed above) it would have been obvious to substitute G-CSF for GM-CSF and the substitution would have yielded predictable results to one of skill in the art at the time of the invention.

Regarding claim language, it is noted that section 2106 of the MPEP states:

> Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation.

In the instant case, claims 18-21 recite 'that provides...' which does not limit the claim to a particular structure and does not limit the claim. Regarding method claims, claim 22 for example recites 'for increasing the numbers of ...' which does not result in a structural or manipulative difference (see section 2111.02 of the MPEP) and therefore does not limit the claim. The composition of Bahlmann and Robinson meet the structural limitations of the claims so the composition must necessarily meet the functional limitations (see MPEP 2112.01).

Response to Amendment/Arguments – 103 Bahlmann and Robinson

Applicants have amended claims 1 and 11, for example. Applicants argue that the composition taught by the combination of Bahlmann and Robinson also includes EPO. Applicants argue that EPO is a utility altering ingredient. Applicants argue that the composition of Bahlmann and Robinson is useful for a different purpose and therefore teaches away from the current invention. Applicants also argue that the method is for a different purpose and therefore teaches away.

The arguments have been fully considered but they are not persuasive. Previously, claim 1 read on a combined preparation containing G-CSF and PlGF. The term containing is synonymous with comprising (MPEP section 2111.03) and therefore the preparation was open-ended. Applicant has amended claim 1 to read on 'a composition consisting essentially of'. Regarding this type of language, section 2111.03 of the MPEP states:

> The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention.
> For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."

In the instant case, there is no clear indication in the specification or claims as to what the basic and novel characteristics are. Therefore, "consisting essentially of" will be construed as equivalent to "comprising". As such, the claimed compositions are open-ended and the compositions are open to have other components such as EPO. Additionally, section 2111.03 states that the applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. It is noted that even though applicant submit that EPO is a utility altering ingredient, mere argument cannot take the place of evidence (see MPEP 2145). Applicant has not shown how the components would materially change the characteristics. It is noted that claim 11 has been amended to recite a method comprising administering G-CSF and PlGF. The language of the claim is such that the composition is open-ended. The method is also open-ended to comprising various steps.

In response to applicant's argument that the intended use is different, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Further, 'the mobilization of peripheral blood progenitor cells' that applicant refers to as the intended use is not even claimed in claim 1, for example. Regarding method claims, claim 22 for example, recites 'for increasing the numbers of ...' which does not result in a structural or

manipulative difference (see section 2111.02 of the MPEP) and therefore does not limit the claim.

For these reasons and the reasons set forth previously, claims 1,3, 11, 13,18-25 are rejected.

Claim Rejections - 35 USC § 103 (Bahlmann, Robinson and others)

(Maintained in part/Necessitated by amendment) **Claims 1,3-5, 11-14,18-25** are rejected under 35 U.S.C. 103(a) as being unpatentable over Bahlmann et al., Robinson et al., Carmeliet et al., Freireich et al., and Kadar et al.

Since the claims have been amended and new claims have been added, the updated rejection is recited below.

As discussed above, Bahlmann and Robinson render obvious claims 1,3, 11, 13-14,18-25.

Bahlmann and Robinson do not expressly teach the recombinant forms of G-CSF and PlGF of claim 4 of the current invention, or the doses of claims 5,12,14 of the current invention.

Robinson et al. teach that recombinant versions of G-CSF and GM-CSF are commonly used, specifically the human versions (abstract). Kadar et al. teach G-CSF use for cell mobilization (as taught by Robinson see above) and teach a specific dosage of 5ug/kg/day (page 611 abstract) twice a day for a total of 10ug/kg/day (compare claim 5,12 of the current invention). Carmeliet et al. teach PlGF (specifically human PlGF column 6 line 9) use as part of treatments such as for transplantations (column 3 line 22) and specifically teach that recombinant PlGF is used (column 15 line 7) and PlGF dosages 'of 15ug/kg/day of active ingredient up to 100 ug/kg/day or higher' (column 15 line 12) are deemed to be a safe level. Freireich et al. teach that

doses of ingredients can be varied appropriately based on the patient and that quantitative calculations can be used as a starting point followed by routine optimization of dose amounts (page 220 2nd column 3rd paragraph).

It would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g.doses), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2145.05).

In relation to KSR, discussed above, it would have been obvious to substitute a recombinant form of either hG-CSF or hPlGF for the G-CSF or PlGF described above. The substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Response to Amendment/Arguments – 103 Bahlmann, Robinson and others

Applicants argue that Bahlmann and Robinson fail to teach the present invention and that the other references fail to rescue the deficiencies. Applicants argue that the references fail to teach a composition or method using a composition with PlGF and G-CSF without additional ingredients.

The arguments have been fully considered but they are not persuasive. Previously, claim 1 read on a combined preparation containing G-CSF and PlGF. The term containing is synonymous with comprising (MPEP section 2111.03) and therefore the preparation was open-

ended. Applicant has amended claim 1 to read on 'a composition consisting essentially of'. Regarding this type of language, section 2111.03 of the MPEP states:

> The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention.
> For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising."

In the instant case, there is no clear indication in the specification or claims as to what the basic and novel characteristics are. Therefore, "consisting essentially of" will be construed as equivalent to "comprising". As such, the claimed compositions are open-ended and the compositions are open to have other components such as EPO. Additionally, section 2111.03 states that the applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. It is noted that even though applicant submit that EPO is a utility altering ingredient, mere argument cannot take the place of evidence (see MPEP 2145). Applicant has not shown how the components would materially change the characteristics. It is noted that claim 11 has been amended to recite a method comprising administering G-CSF and PlGF. The language of the claim is such that the composition is open-ended. The method is also open-ended to comprising various steps.

For these reasons and the reasons set forth previously, claims 1,3-5, 11-14,18-25 are rejected.

Claim Rejections - 35 USC § 103 necessitated by amendment

(Necessitated by amendment) **Claim 26** is rejected under 35 U.S.C. 103(a) as being unpatentable over Bahlmann et al., Robinson et al., and Swain (Pharmaceutical and Medical Packaging news magazine published august 1999).

As discussed above, Bahlmann and Robinson render obvious compositions comprising G-CSF and PlGF.

Bahlmann and Robinson do not expressly teach G-CSF and PlGF as part of a kit.

Swain teach (2nd paragraph) 'that packaging can add to the bottom line by attracting consumers and healthcare practitioners, by cutting pilfering and counterfeiting, by adding to product shelf lives, and by improving patient compliance with drug regimes'. Swain also teach that packaging enhances ease of use and the aesthetic value.

Since Bahlmann teach administration to patients, one would be motivated to package the composition as taught by Bahlmann and Robinson to attract consumers as taught by Swain. Since packaging is well-known in the art (see swain throughout) one would have a reasonable expectation of success. The claim would have been obvious because a particular known technique (packaging as a kit) was recognized as part of the ordinary capabilities of one skilled in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Due to the claim amendments and new claims, a new prior art search was performed. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: US 2004/0248796 (see claim 103 for example).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald T. Niebauer whose telephone number is 571-270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rtn

11/4/07
ANISH GUPTA
PRIMARY EXAMINER